UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,624	01/22/2002	Sean H. Adams	09800081-0066	4963

23552 7590 10/01/2004

MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,624	ADAMS ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-26,30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/18/03,4/14/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1-31 are pending.

In response to a restriction requirement, Applicants elected with traverse Groups XXV-XXVII in a communication filed on 7/26/2004. In view of the fact that more than one invention was elected and to expedite prosecution of the instant application, the Examiner contacted Katherine Kowalchyk on 8/10/2004 for a telephonic election of a single invention. Applicants elected with traverse Group XXV, claims 27-29 drawn in part to a method of screening a patient for a metabolic disease with a polypeptide comprising SEQ ID NO: 2. Applicant's traverse of the restriction requirement is on the same ground(s) indicated in a communication filed on 7/26/2004.

Applicant's traverse is on the ground(s) that there are not sufficient reasons and/or examples to justify the requirement. Applicants submit that it would not be unduly burdensome to search Groups XXVIII-XXX since search of Group XXV is likely to uncover subject matter covered in Groups XXVIII-XXX.

Applicant's arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement. As indicated previously, inventions XXV-XXX are deemed unrelated as they are not disclosed as being used together, have different modes of operation, different functions or different effects. In particular, the methods of inventions XXV-XXX comprise different steps, may use different products and produce different results. The methods of Groups XXV-XXVII require either measuring mRNA or measuring the amount of a polypeptide. The methods of Groups XXVIII-XXX require comparing the polynucleotides of SEQ ID NO: 1, 3, or 5 to a gene encoding a brown fat inducible thioesterase (BFIT) and they do not require using BFIT polypeptides. In regard to arguments that a search of Groups XXV-XXX would not impose an undue burden of search on the Office, this is not found persuasive since a comprehensive search of all groups would require not only different sequence searches

but also patented/non-patented literature searches, as well as class/subclass searches which are not co-extensive. In addition, while literature disclosing a polypeptide may provide information in regard to the corresponding polynucleotide, it is false to assume that the same literature will provide information regarding methods of use for the polynucleotides or polypeptides or that literature which provides information regarding one method of use for a product will provide information regarding other methods of use for that product.

The requirement is deemed proper and therefore is made FINAL.

Claims 1-26 and 30-31 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

It is noted that when referring to specific sections of the specification, the Examiner will use the corresponding published application, i.e. U.S. publication No. 2003/0220238.

Specification

1. The specification is objected for not complying with sequence rules. While Figure 2 displays alignments of several sequences, neither the drawings nor the Brief Description of the Drawings indicate the corresponding sequence identifiers. Applicant is required to insert the corresponding sequence identifiers in the Brief Description of the Drawings or amend the drawings to include the sequence identifiers in front of each sequence. See particularly 37 CFR 1.821(d). Appropriate correction is required.

Priority

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/263,362 filed on 01/22/2001.

3. SEQ ID NO: 1 and 2 appear to have been disclosed in provisional application No. 60/263,362 filed on 01/22/2001.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on 2/18/2003 and 4/14/2003 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Claim Objections

5. Claims 27-29 are objected to because of the recitation of "BFIT". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. It is suggested that the term "brown fat inducible thioesterase" be recited at least once next to the term "BFIT". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 27-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 27-29 are indefinite since they omit essential steps in the claimed method. Claims 27-29 are directed to a method of screening a patient for a metabolic disease. However there is no step indicating how measuring BFIT expression in a tissue sample correlates with the screening of a patient for a metabolic disease. Correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 27-29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

Claims 27-29 are directed to a method of screening a patient for a metabolic disease wherein said method comprises measuring the expression of any brown fat inducible thioesterase gene or measuring the levels of any brown fat inducible thioesterase polypeptide. While the specification discloses that (1) "metabolic diseases" include obesity, wasting disorders such as cachexia, and diabetes (paragraph [29]) , (2) the chromosomal position of the BFIT gene in mice was co-localized with chromosomal markers associated with body fat (paragraph [164]), (3) BFIT in mice is induced by exposure to cold and repressed by warm temperature (paragraph [162]), and (4) obese-prone mice fed a high fat diet showed increased expression of BFIT as opposed to obese-resistant mice fed with a high fat diet (paragraph [164]), the claimed invention does not meet the utility requirements as the specification fails to disclose a correlation between BFIT gene expression and any metabolic disease in humans, including obesity. The asserted utility for the claimed method, i.e. screening a patient for a metabolic disease, is not specific or substantial. In regard to obesity, it is assumed that the claimed method encompasses screening a patient for a predisposition to obesity, and not screening a patient for obesity, since screening for obesity would only require measuring an individual's weight and height followed by a determination as to whether that individual's weight fall within a predetermined normal range for that height. It is noted that while the specification shows that obese-prone mice fed a high fat diet showed increased gene expression of BFIT as opposed to obese-resistant mice fed with a high fat diet, there is no indication that obese-prone mice show increased gene expression of BFIT as opposed to obese-resistant mice in the absence of a high fat diet. As such, it is unclear as to how one can screen a patient with a predisposition for obesity if it there is

no evidence indicating that changes in gene expression of BFIT correlate with such predisposition. Furthermore, if the intended use for the claimed method is to screen obese patients by measuring BFIT gene expression to determine the underlying cause of that patient's obesity, it is noted that there is no evidence in the specification which shows whether a reduction in gene expression of BFIT correlates with any particular type of obesity or a particular disorder which would lead to obesity.

Applicant's asserted utility for the claimed method, particularly in view of a lack of knowledge as to a correlation between gene expression of BFIT and any human metabolic disease, including a predisposition to obesity, or a correlation between a reduction in BFIT gene expression and a particular type of obesity or a particular disorder which would result in obesity, constitutes a utility that requires further research to identify or reasonably confirm a "real world" context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). This type of utility is not considered a "substantial utility". While an assay that detects the presence of an agent that has a stated correlation to a predisposition to the onset of a specific disease condition would be considered a "substantial utility" in the context of identifying potential candidates for preventive measures, in the instant case the BFIT genes disclosed and their products are suitable only for additional research to determine if there is a correlation between their expression and any human metabolic disease. Thus, for the reasons set forth, the claimed method does not have a real-world use and does not meet the utility requirements under 35 USC 101.

11. Claims 27-29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, First Paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

14. Claims 27-29 are directed to a method of screening a patient for a genus of metabolic diseases wherein said method comprises measuring the expression of a genus of brown fat inducible thioesterase genes or measuring the levels of a genus of brown fat inducible thioesterase polypeptides. While the specification discloses the polynucleotides of SEQ ID NO: 1, 3, and 5 as encoding two human and one mouse brown fat inducible thioesterases (SEQ ID NO: 2, 4, and 6, respectively), and discusses a potential linkage between BFIT gene expression and obesity, the specification is completely silent in regard to a correlation between BFIT gene expression and other metabolic diseases, and the structures of other BFIT genes and BFIT polypeptides. The specification also fails to disclose (a) the structural elements required in any BFIT gene or any BFIT polypeptide, or (b) the structural elements present in the polynucleotides of SEQ ID NO: 1, 3, or 5 or the polypeptides of SEQ ID NO: 2, 4, or 6 which should be present in any polynucleotide or polypeptide to display the required functional characteristics.

The genus of polynucleotides and polypeptides required to practice the claimed method is a large structurally variable genus. While a sufficient written description of a genus of polynucleotides/polypeptides may be achieved by a recitation of a representative number of species defined by their sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, there is no structural feature which is representative of all the members of the genus of BFIT genes or BFIT polypeptides recited in the claims. Furthermore, while one could argue that the recited genus of polypeptides/polynucleotides is

adequately described by the polynucleotides of SEQ ID NO: 1, 3, 5 or the polypeptides of SEQ ID NO: 2, 4, 6, since one could use structural homology using the disclosed structures and those known in the art to isolate other BFIT genes and BFIT polypeptides as required by the claimed method, it is noted that the art teaches the unpredictability of using structural homology to accurately determine function and even a high degree of structural homology may not result in functional homology. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Therefore, in the absence of any additional information correlating structure with BFIT activity, or any correlation between the polypeptides of SEQ ID NO: 2, 4, 6 and BFIT activity, many structurally unrelated polypeptides/polynucleotides are encompassed by the genus. The specification only discloses a few species of the genus, i.e. SEQ ID NO: 1-6, and discusses a potential linkage between BFIT gene expression and obesity, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus of polypeptides/polynucleotides and metabolic diseases required in the claimed method. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

15. Even if specific and substantial utility or well established utility is found for the claimed method, the following rejection applies. Claims 27-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening a patient for obesity predisposition by

measuring the levels of a polypeptide comprising SEQ ID NO: 2, 4, or 6, or measuring the expression levels of a polynucleotide encoding the polypeptide of SEQ ID NO: 2, 4 or 6, does not reasonably provide enablement for a method of screening a patient for any metabolic disease by measuring the levels of any brown fat inducible thioesterase or measuring the expression levels of any brown fat inducible thioesterase gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims, as discussed above, is not commensurate with the enablement provided in view of the large number of undisclosed BFIT genes and BFIT polypeptides required to practice the claimed method and the large number of unknown metabolic diseases which can be screened for with the claimed method. While the polynucleotides of SEQ ID NO: 1, 3, 5 and the polypeptides of SEQ ID NO: 2, 4, 6 have been disclosed, there is no disclosure of (1) all the other BFIT genes and BFIT polypeptides required in the claimed method, (2) structural features common to all BFIT polypeptides, or (3) critical structural elements in the polypeptides of SEQ ID NO: 2, 4, 6 which are required in any protein to display BFIT activity. Furthermore, as previously disclosed, while the specification discusses the potential linkage between BFIT gene expression and obesity, the specification is completely silent in regard to a correlation between BFIT gene expression and other metabolic diseases. The art as discussed above, teaches the unpredictability of isolating proteins of similar function based solely on structural homology and indicates that even high structural homology does not always results in functional

homology. Since structure determines function, one of skill in the art would require some knowledge or guidance as to which are the structural elements in a protein which are characteristic of BFIT activity. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the metabolic diseases which can be screened for with the claimed method, the lack of knowledge about the critical structural elements required to display the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) screen and isolate those polypeptides/polynucleotides having BFIT activity, and (2) determine the metabolic diseases which can be screened for with the claimed method, to practice the full scope of the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Conclusion

16. No claim is in condition for allowance.

17. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

18. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
September 23, 2004

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600